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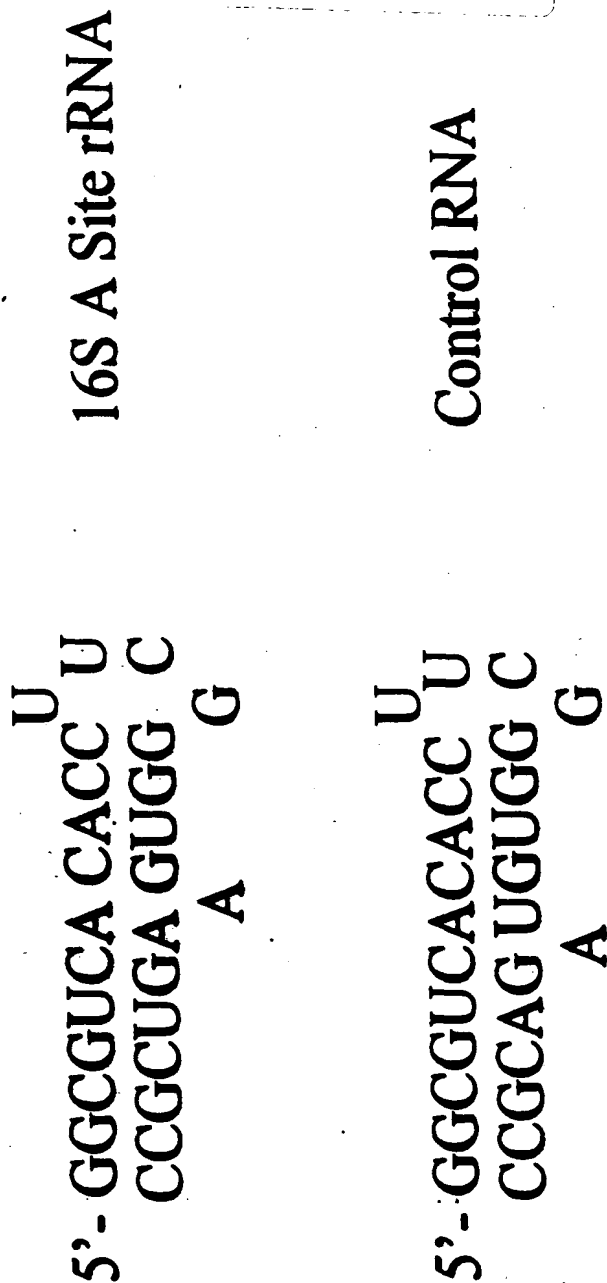


Figure 1. Sequence and structure of 27mer RNA target

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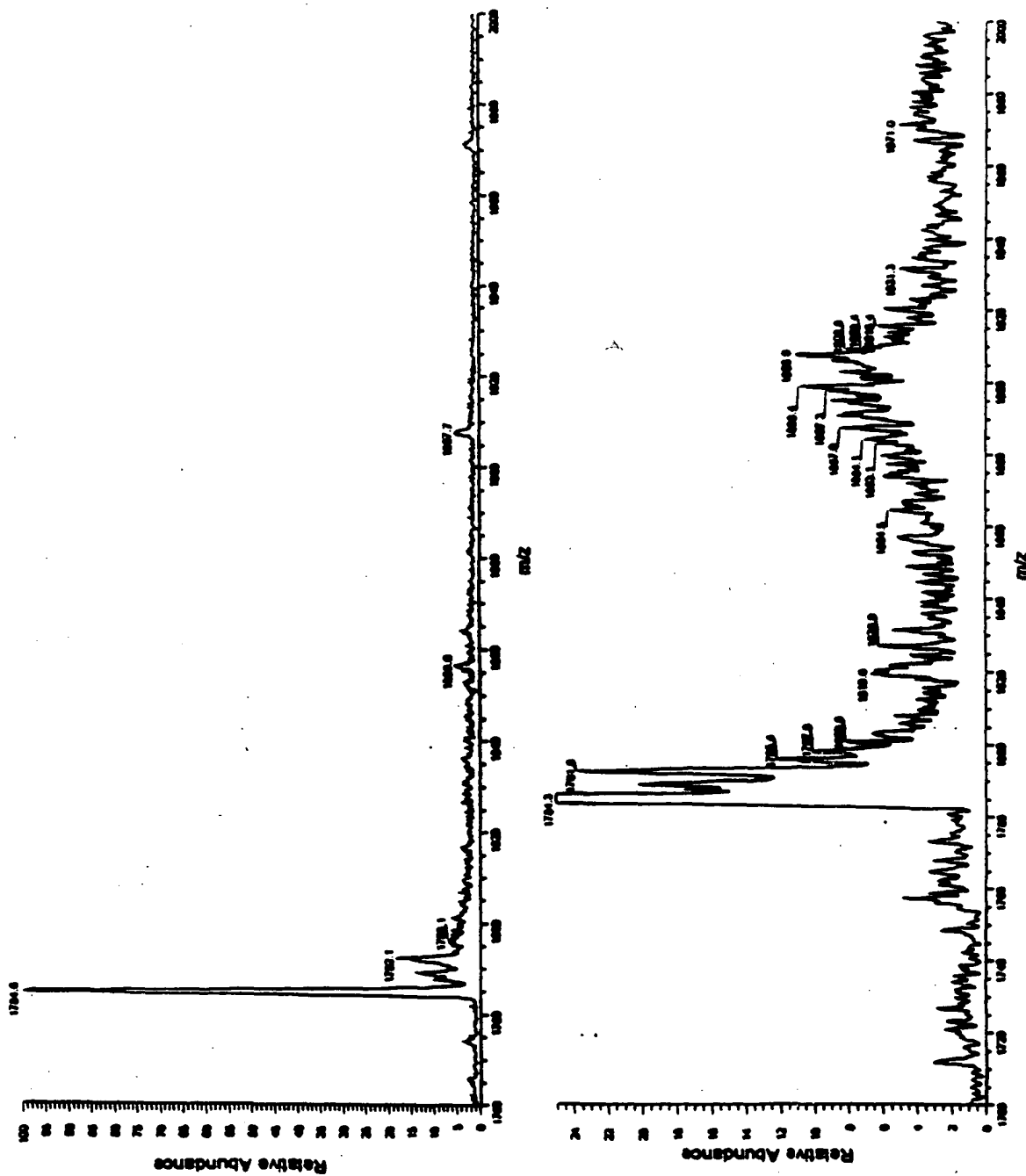
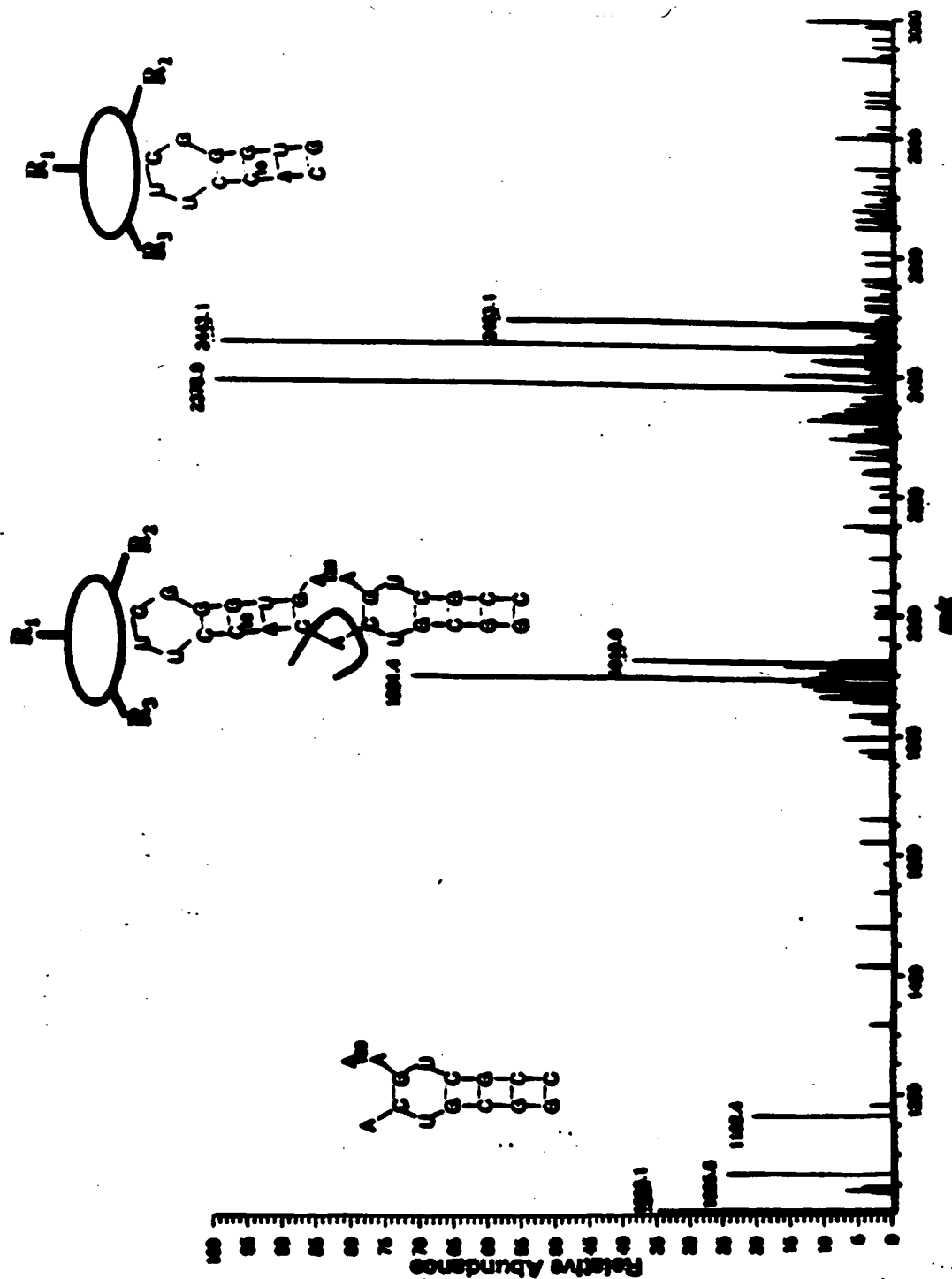


Figure 3. RNA/DNA chimera+paramomycin (upper); chimera+library (lower)

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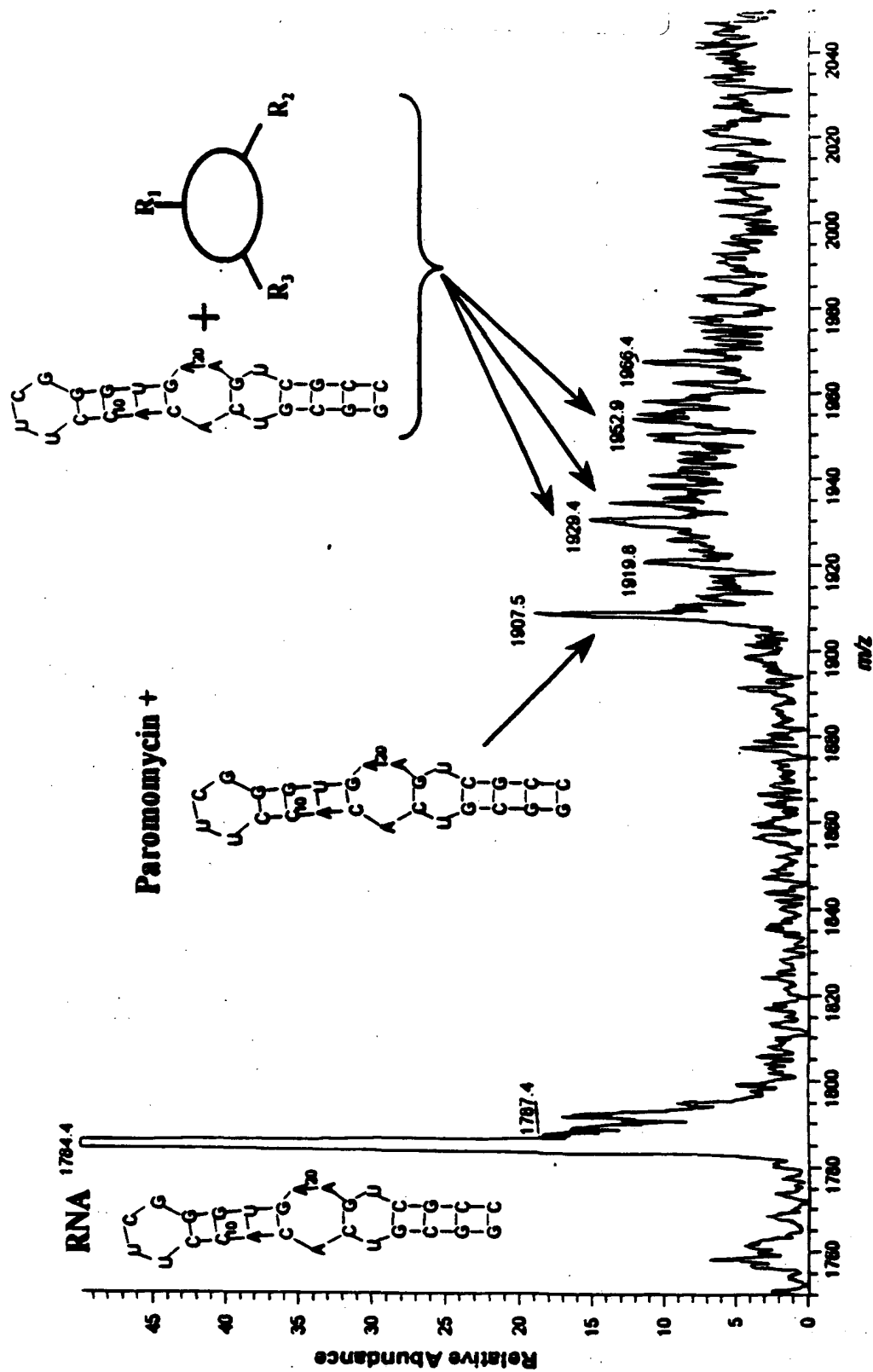


Figure 5. ESI-MS of RNA/DNA chimera bound to paromomycin and library

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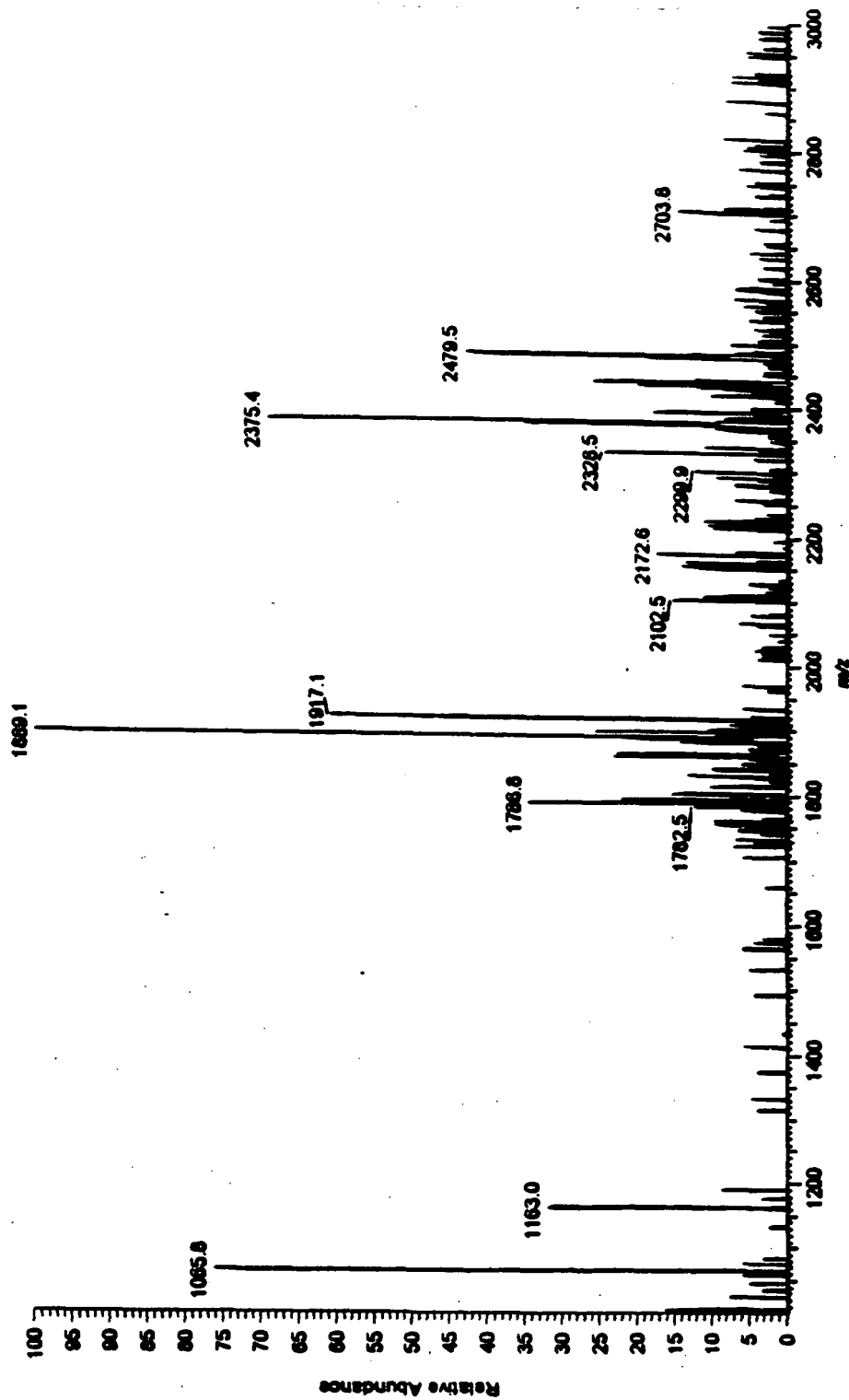


Figure 6. MS/MS of RNA/DNA chimera + compound with mass 665.1 not bound at the A-site

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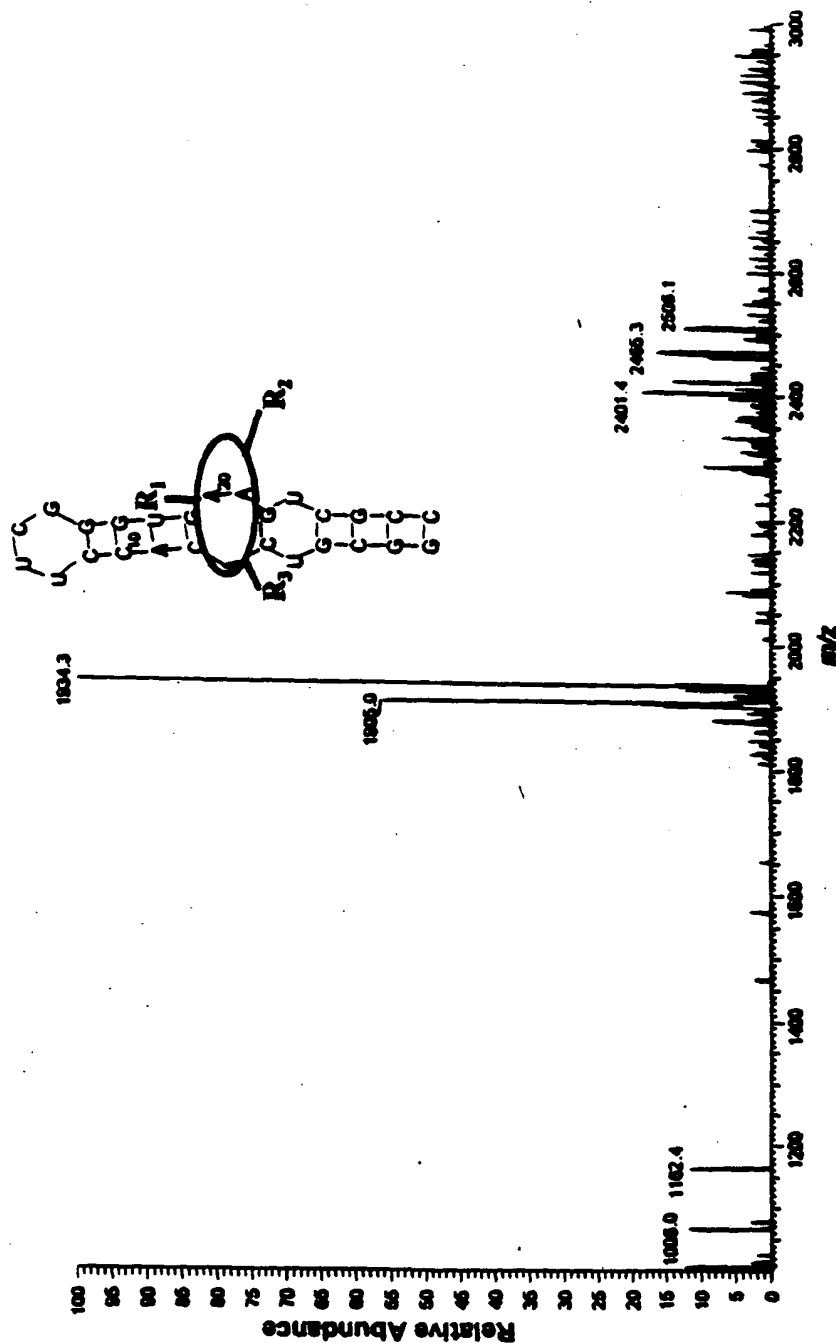


Figure 7. MS-MS analysis of member bound to RNA/DNA chimera at the A-Site



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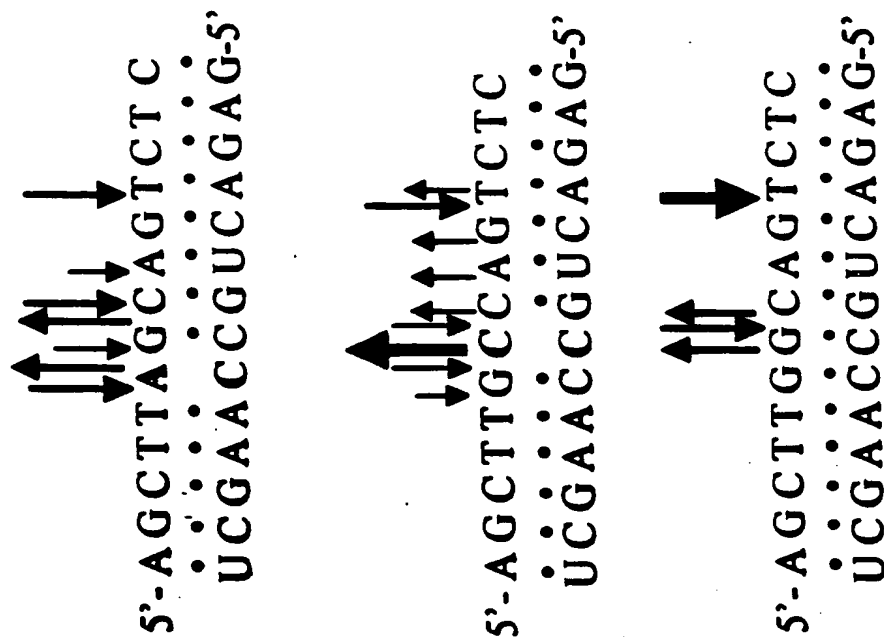
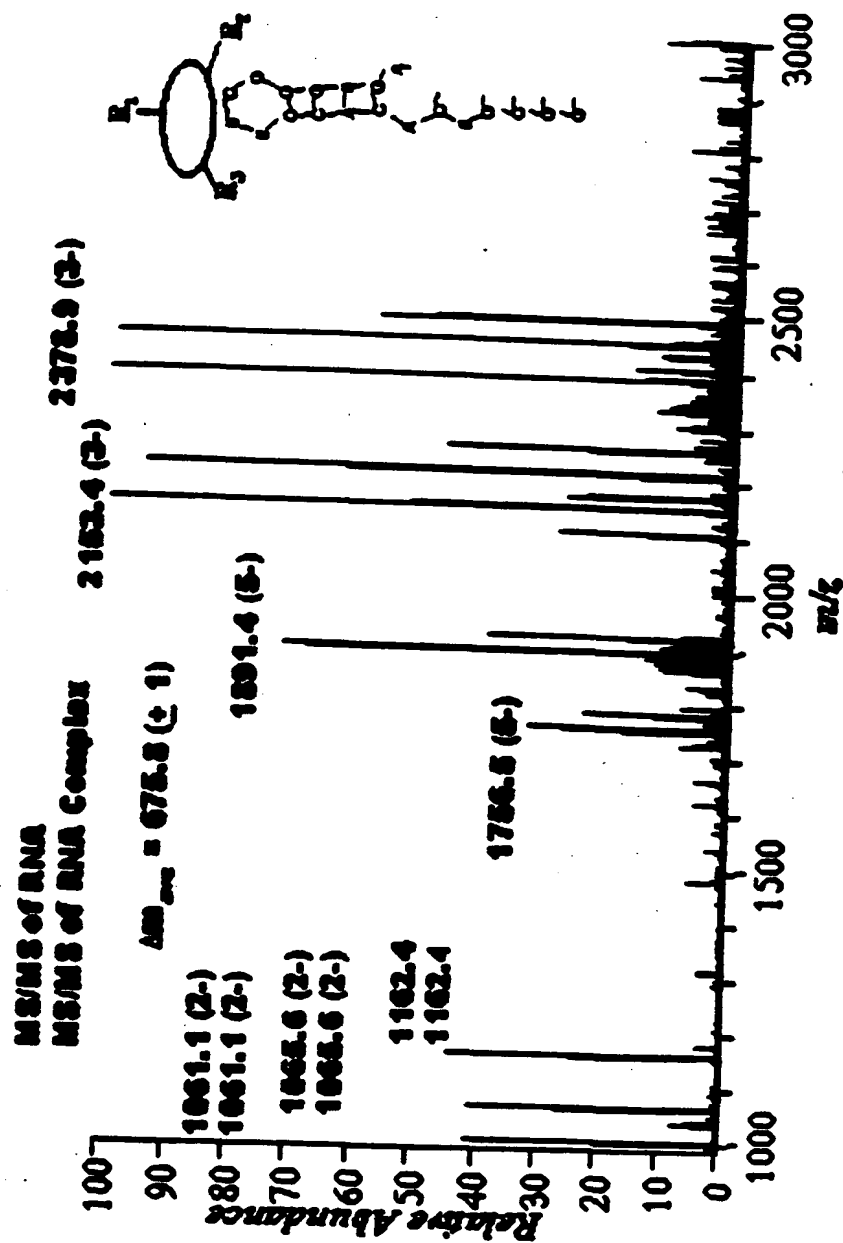


Figure 9. MS Fragmentation of DNA:RNA duplexes

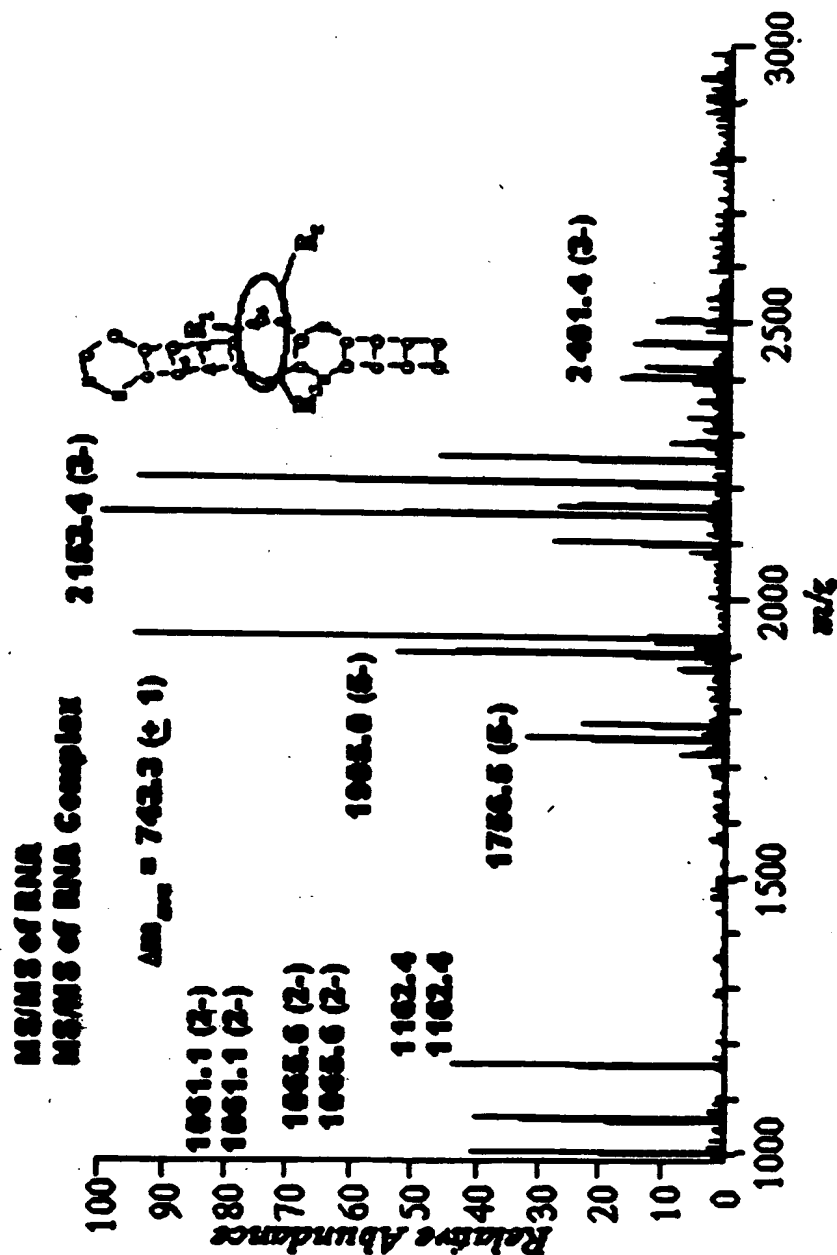
MASS Analysis of Binding Location

FIGURE 10



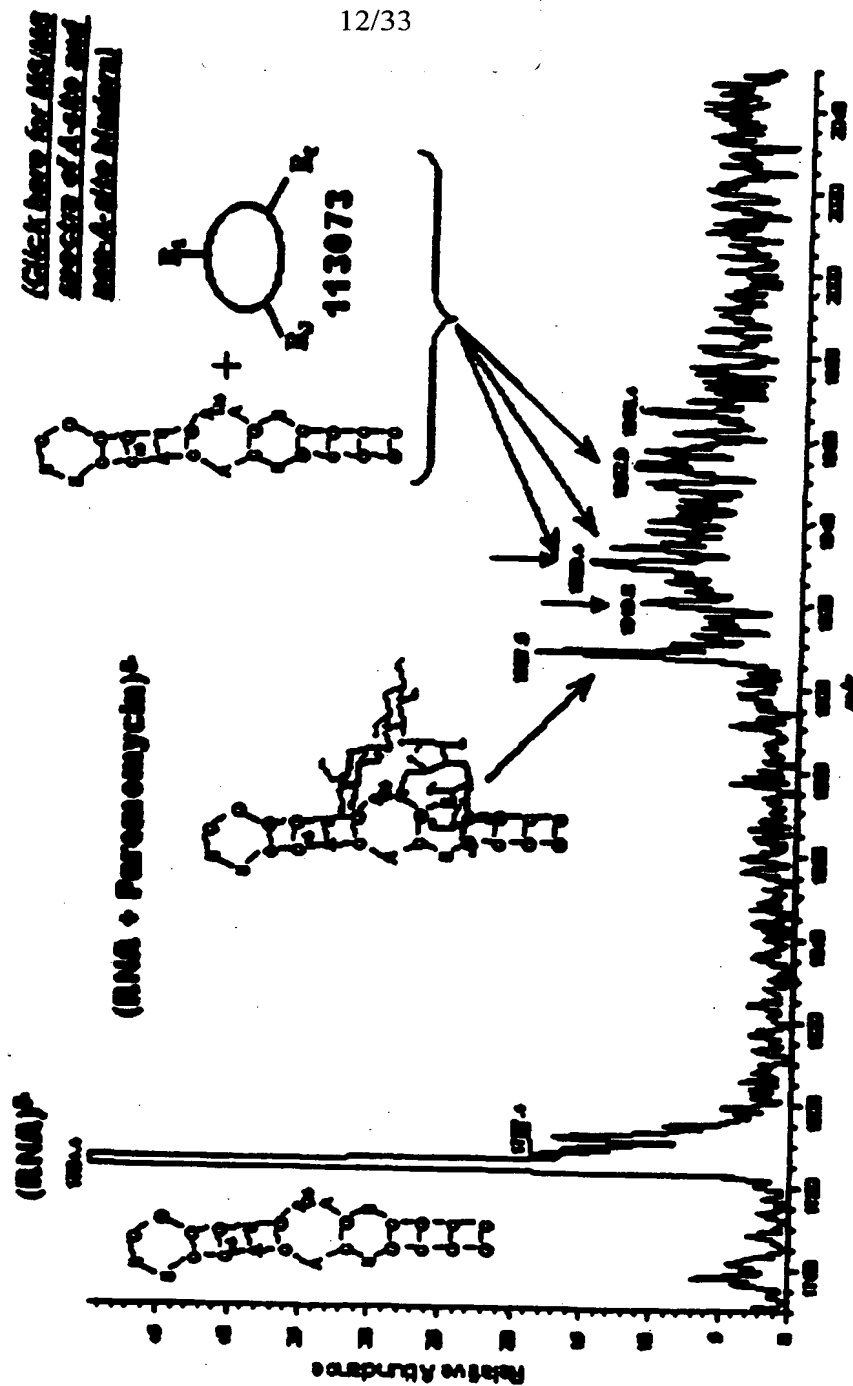
MASS Analysis of Binding Location **non-A site binder**

FIGURE 11



**MASS analysis of 16S A site RNA plus
216 member library
(performed on quadrupole ion trap)**

FIGURE 12

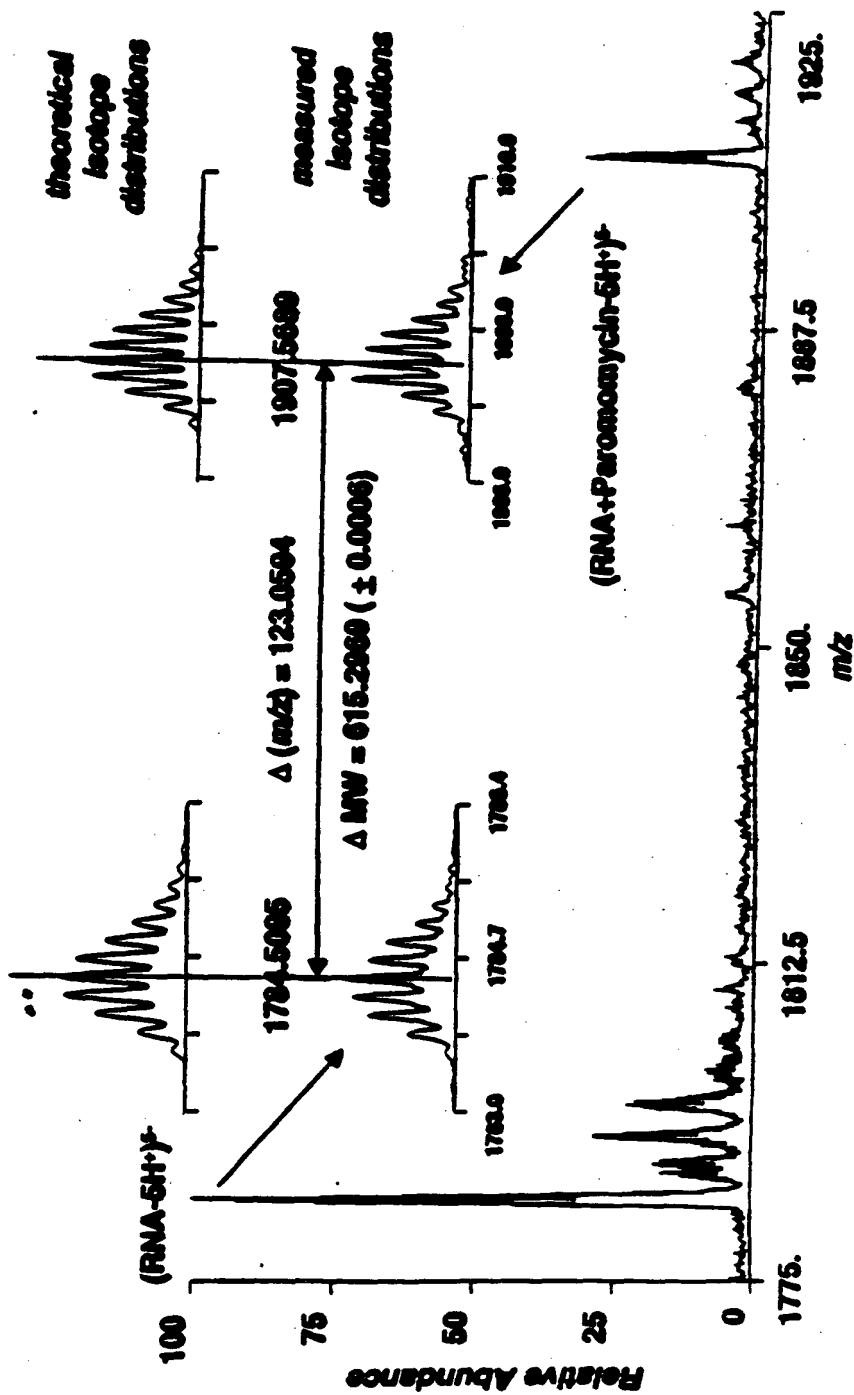


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Figure 13

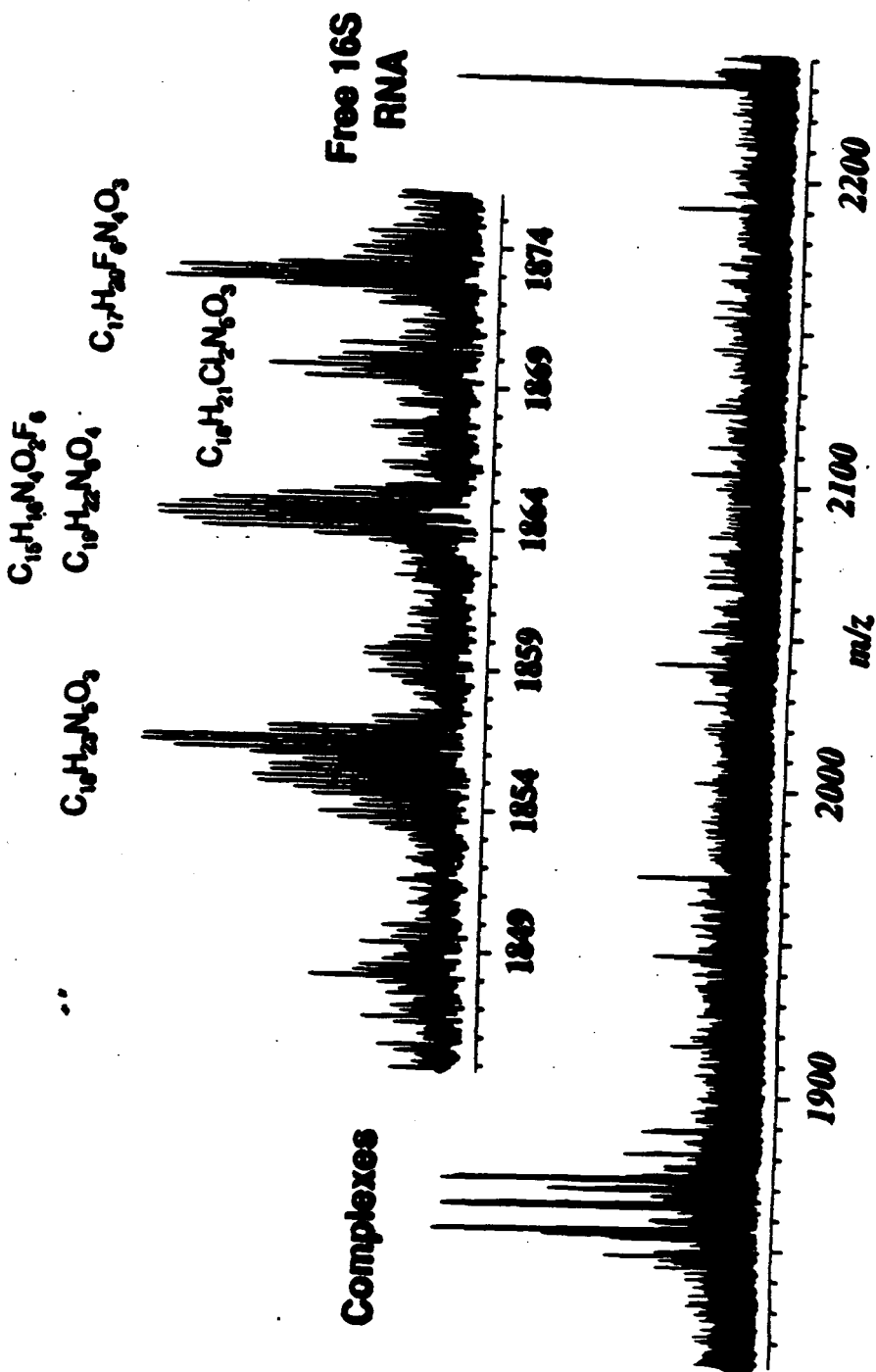
High Precision ESI-FTICR Mass Measurement of 16S A site RNA/Paromomycin Complex

use of unbound RNA as internal mass standard provides low ppm mass measurement errors



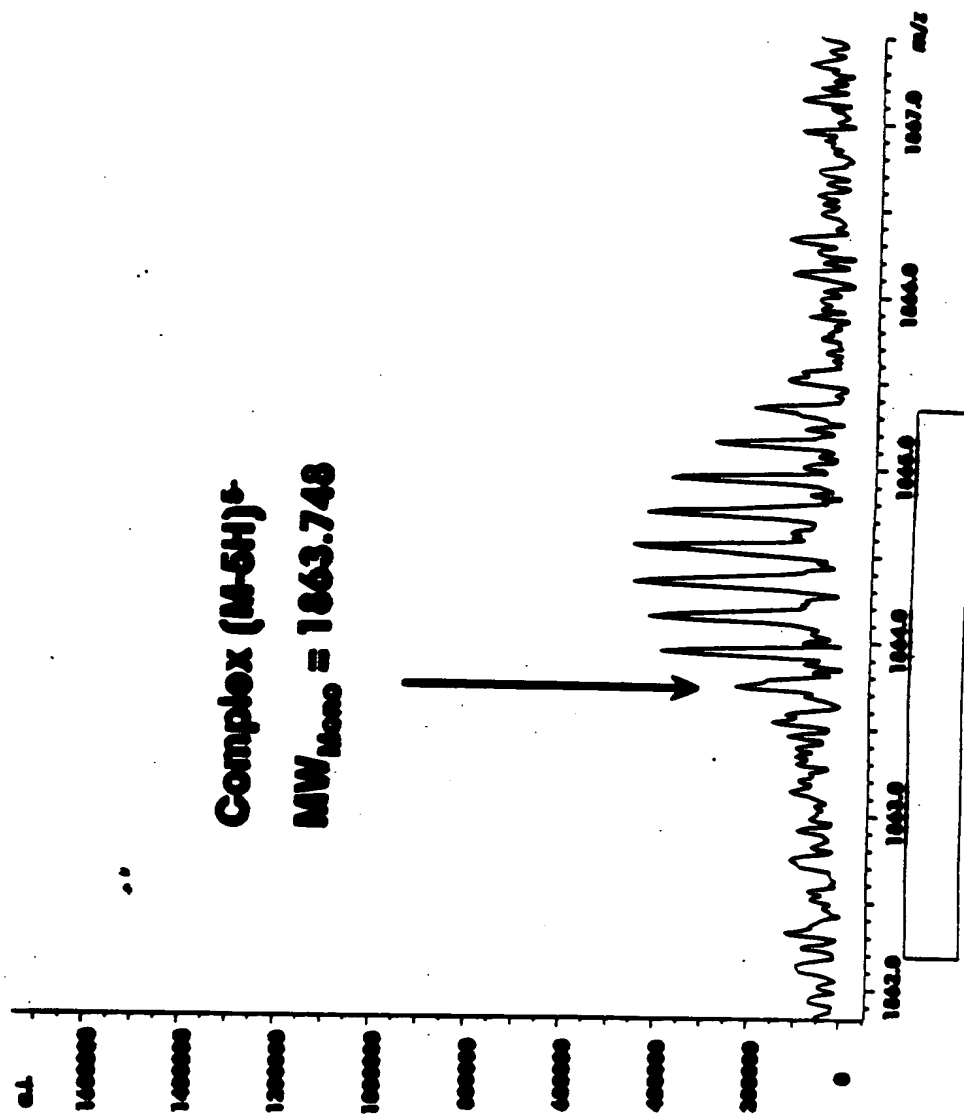
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Figure 14
MASS of 60-Member Ibis Library Against 16S A-site RNA



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Figure 15
MASS of 60-member Library against 16S A-site Model



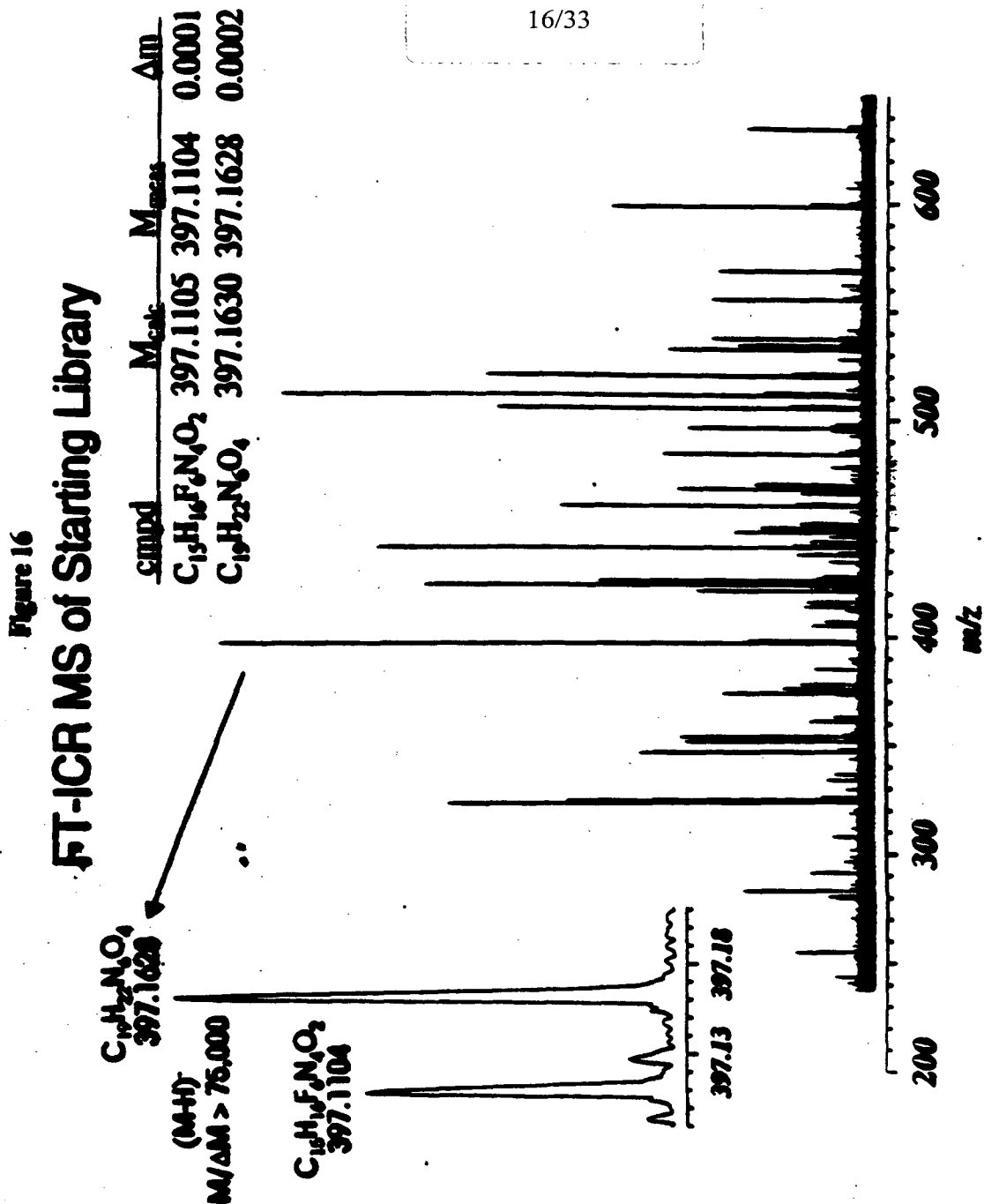
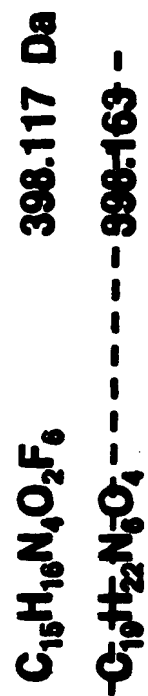


Figure 17
Compound Identification from a 60-member
Combinatorial library with MASS

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Complex M_{mass}	9320.300\pm.009 Da
RNA M_{mass}	8922.189\pm.009
ΔM	398.111\pm.009 Da



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Figure 18

Elemental Composition Constraints

Measured Mass: 615.2969

Mass Tolerance: 1.0 ppm

Charge: 0

Element Min. atoms Max. atoms

¹² C	12	30
¹ H	23	60
¹⁶ O	7	20
¹⁴ N	3	20

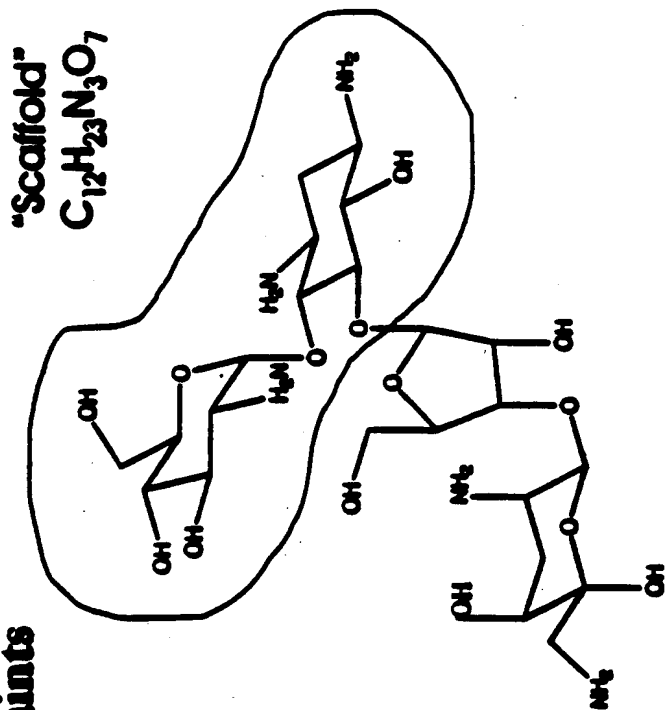
Possible Elemental Compositions:

Calc. Mass Error (ppm) Molecular Formula

615.296291	0.98	¹⁶ O ₄ ¹⁴ N ₁₉ ¹² C ₂₁ ¹ H ₃₃
615.296298	0.98	¹⁶ O ₃ ¹⁴ N ₁₂ ¹² C ₂₂ ¹ H ₃₉
615.296305	0.97	¹⁶ O ₁₄ ¹⁴ N ₅ ¹² C ₂₃ ¹ H ₄₅
615.296808	0.15	¹⁶ O ₁₅ ¹⁴ N ₁₇ ¹² C ₈ ¹ H ₄₁
615.296815	0.14	¹⁶ O ₂₀ ¹⁴ N ₁₀ ¹² C ₉ ¹ H ₄₇

Further constrain by elemental composition of "letters"

unintended products...



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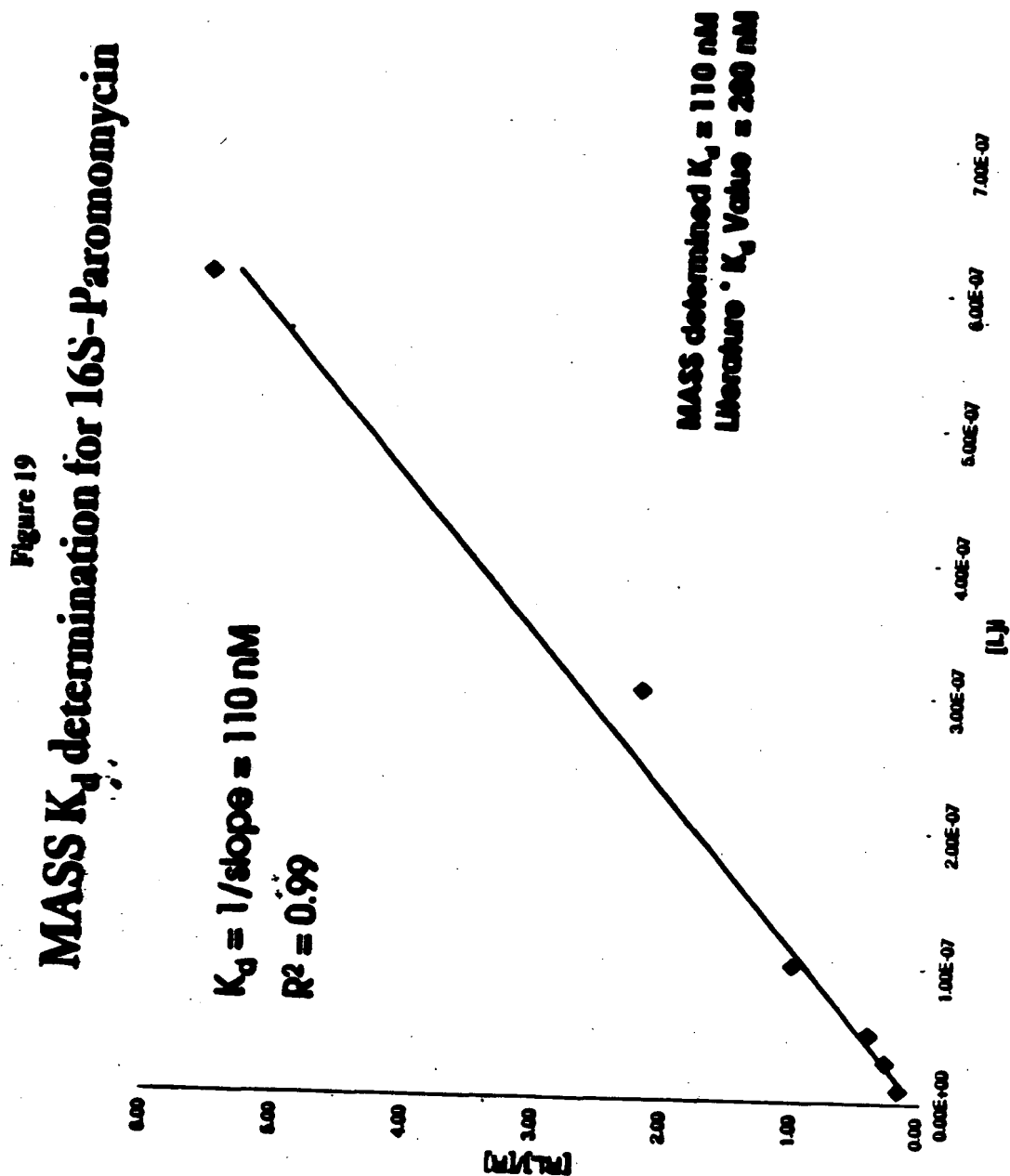
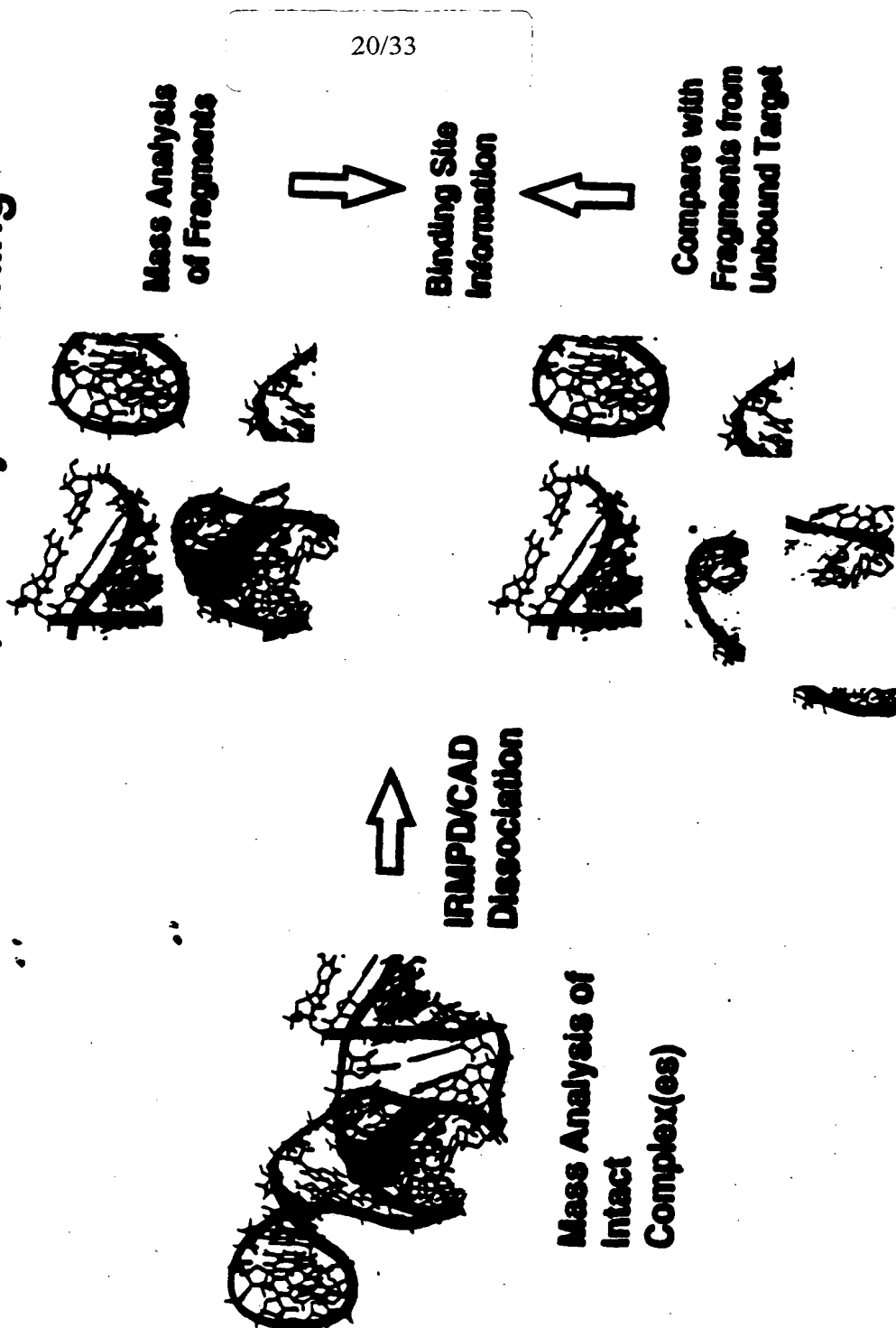
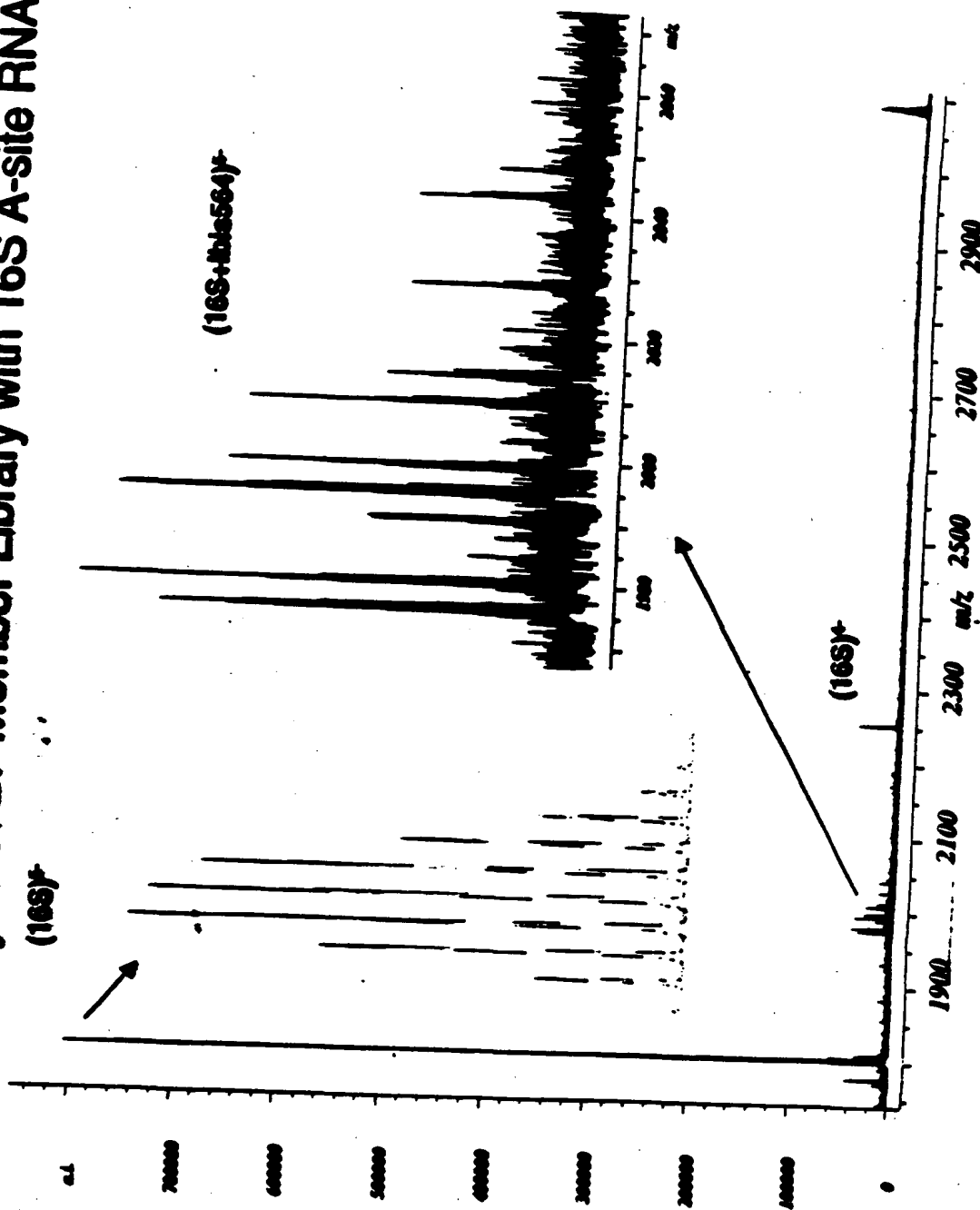


Figure 20
Multitarget Affinity/Specificity Screening



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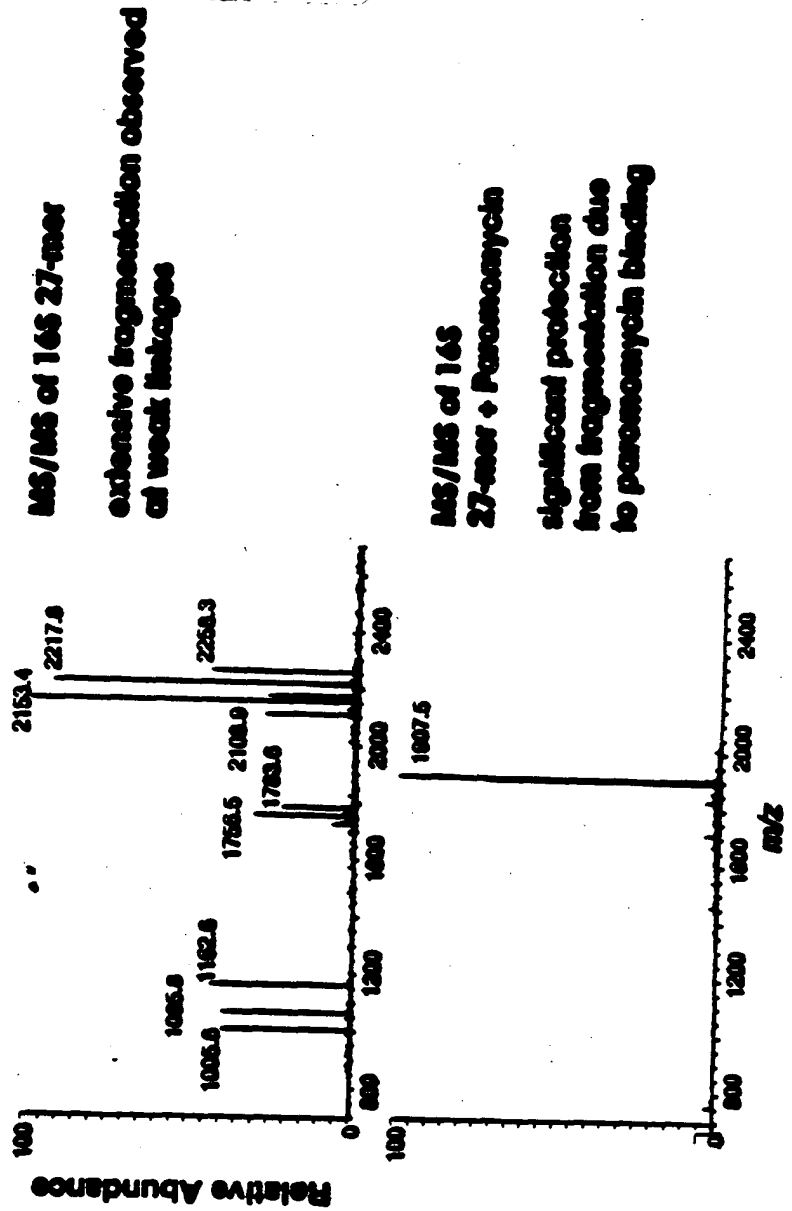
Figure 21 .
MASS Analysis of 27 Member Library with 16S A-site RNA



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Figure 22

MASS Protection Assay



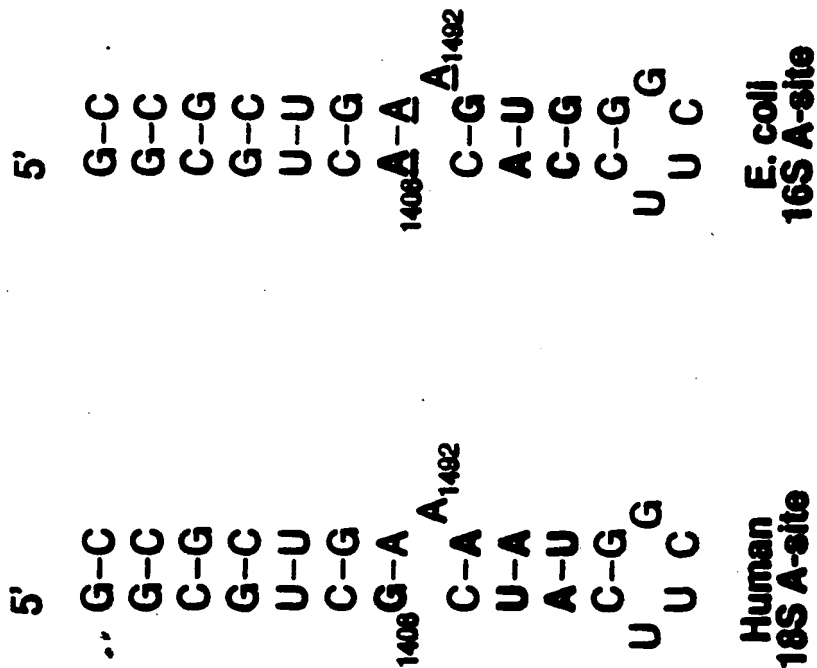
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Figure 23 MASS Protection Assay



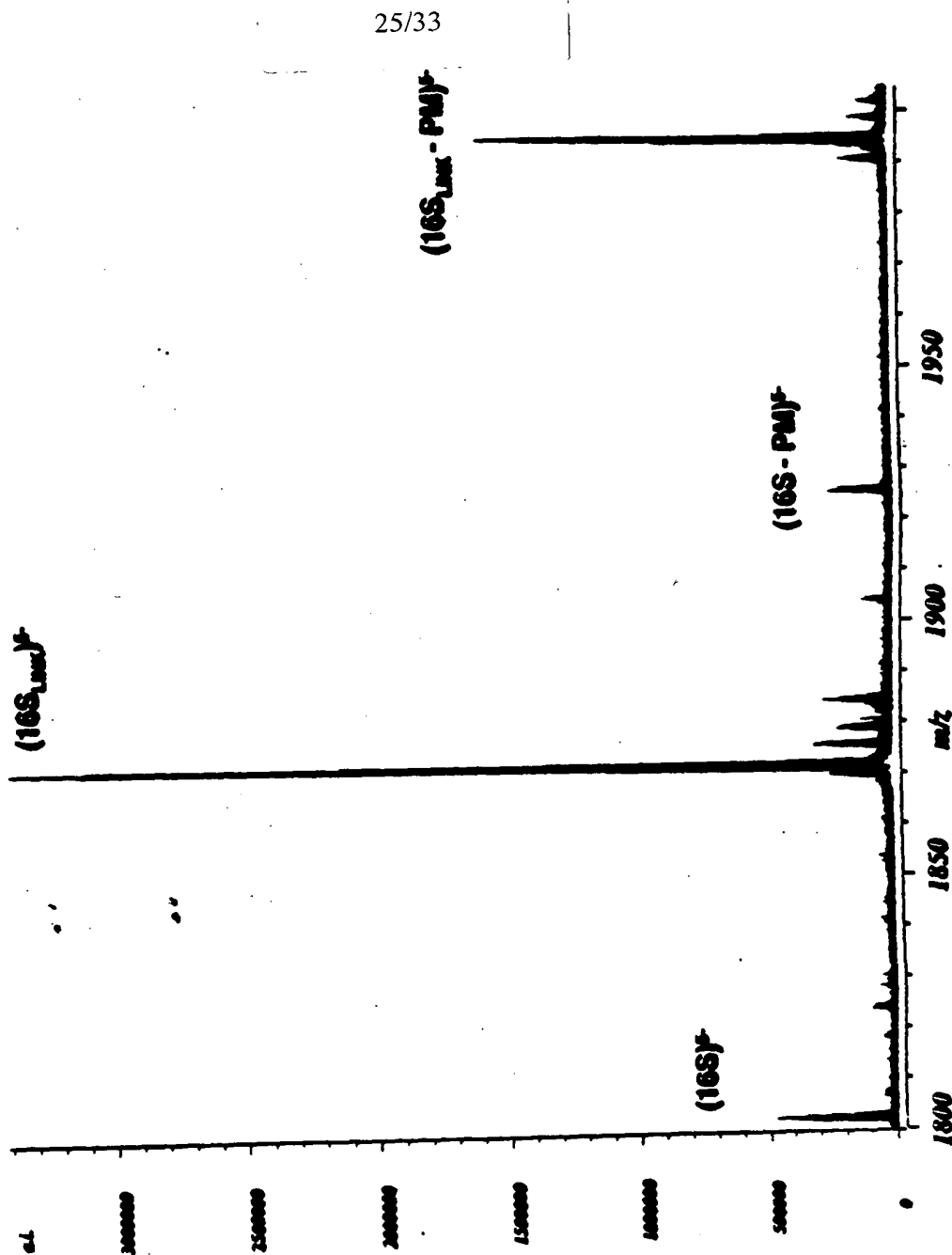
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Figure 24
Eukaryotic and Prokaryotic A-Sites
 Aminoglycoside antibiotics bind to
 A-site of decoding region in 16S RNA



$\Delta MW = 15.011 \text{ Da}$

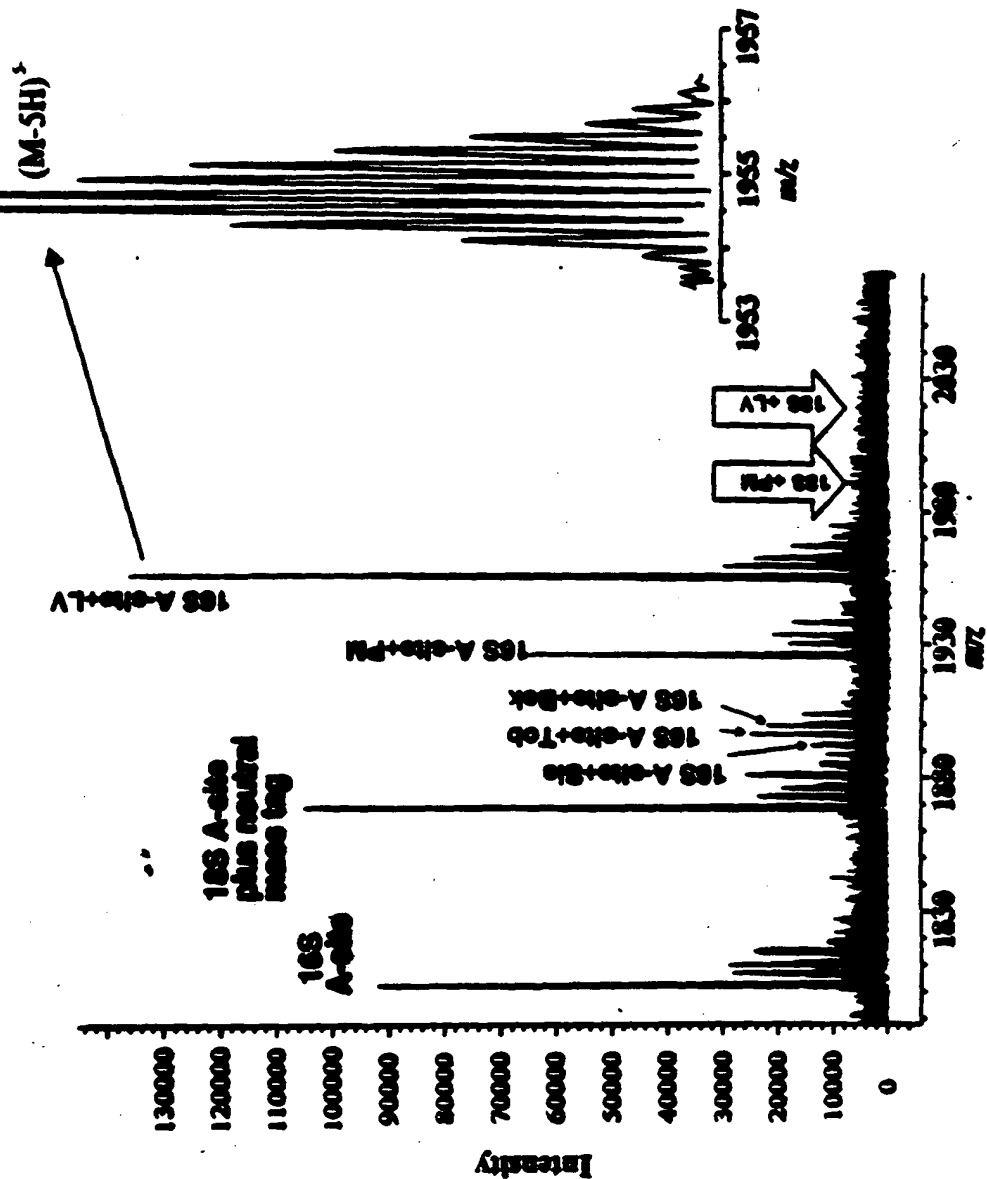
Figure 25
Neutral Mass Tag Does Not Affect Ligand Binding



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Figure 26

Simultaneous Screening of 16S A-site and 18S A-site Model RNAs Against Aminoglycoside Mixture



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Figure 27

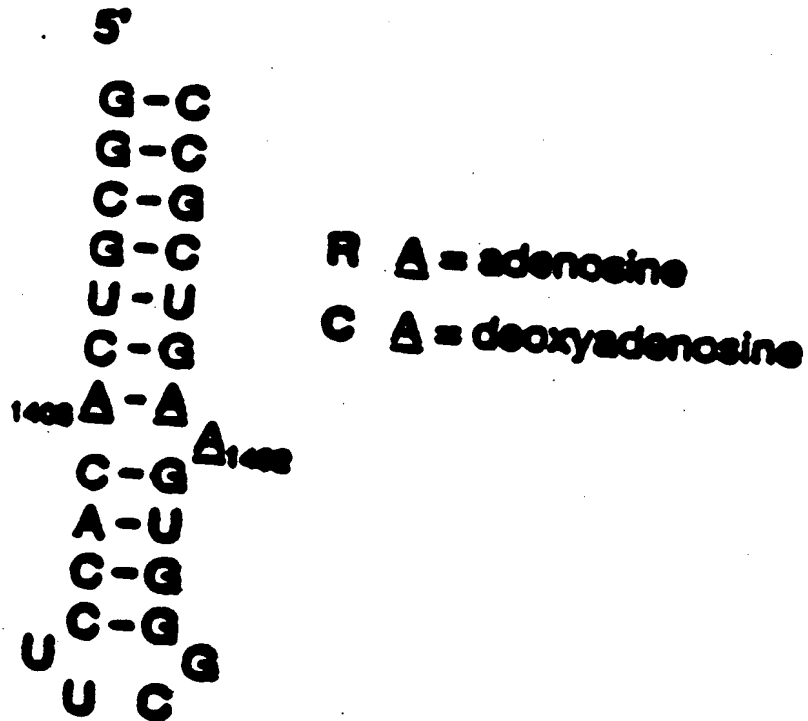
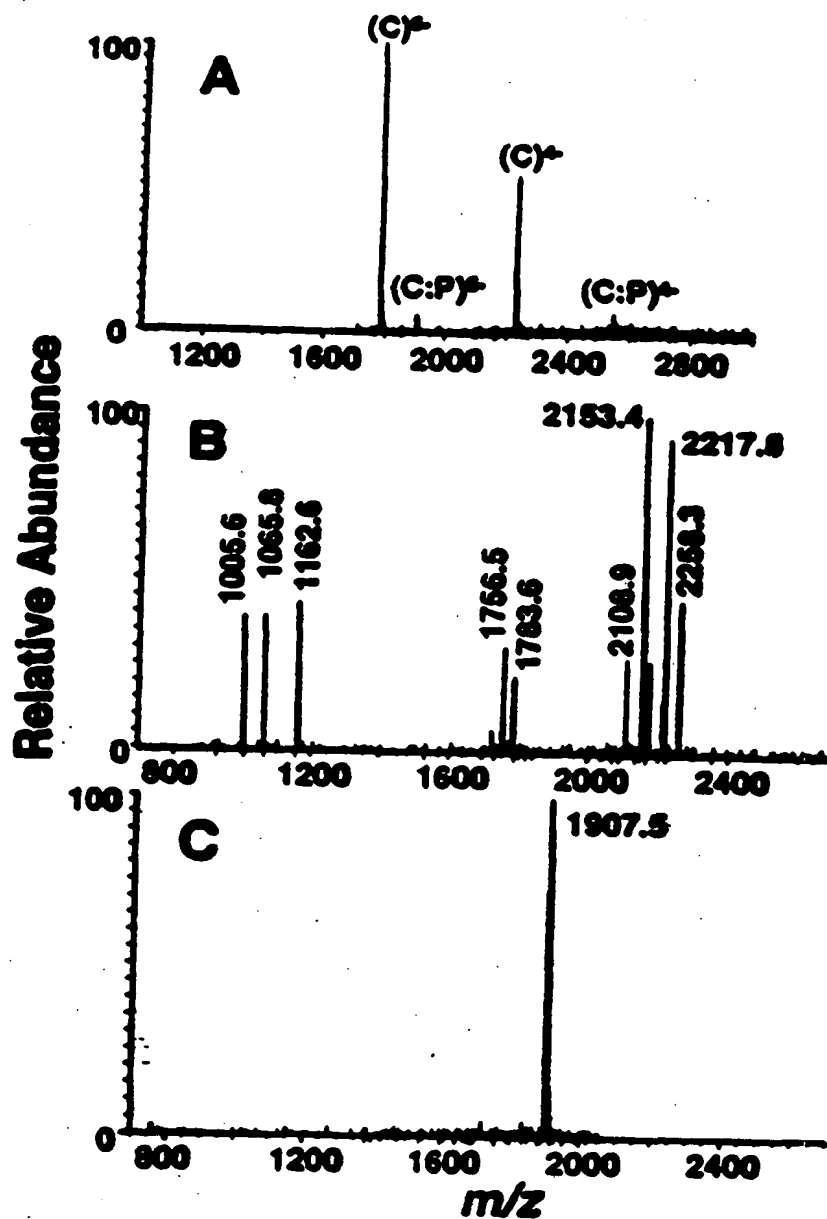


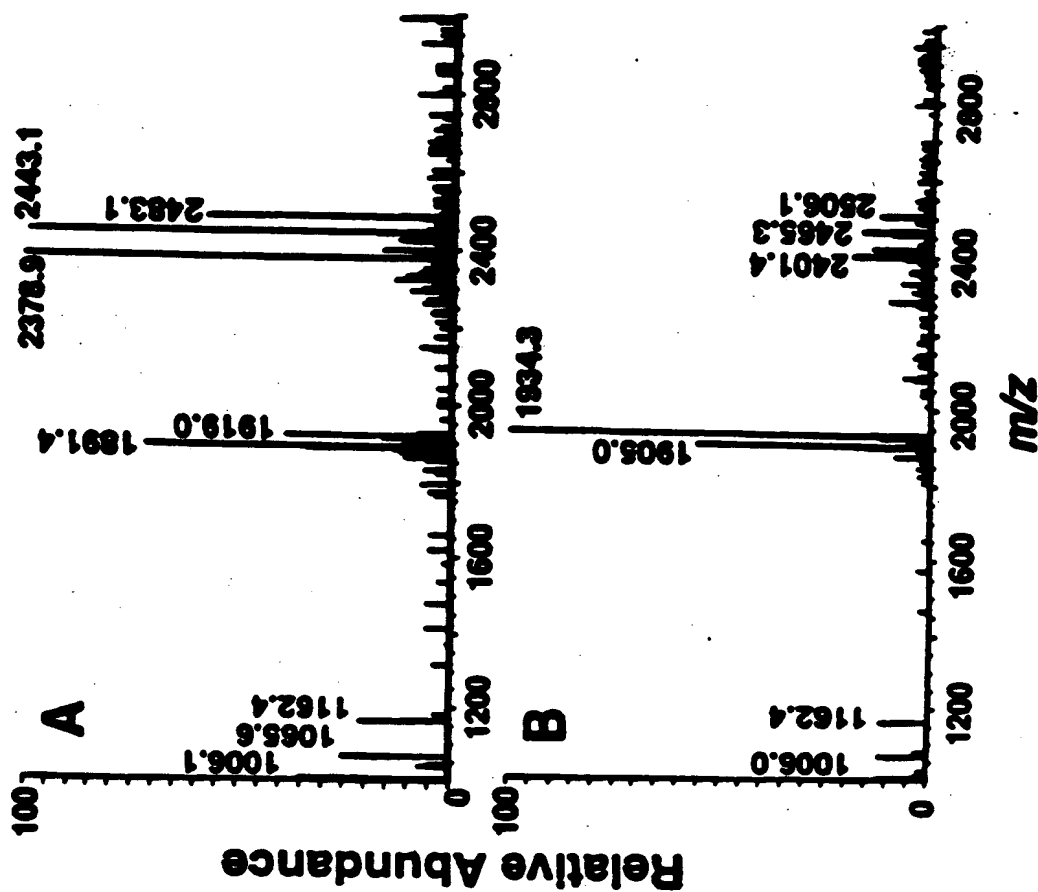
Figure 28

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Figure 29



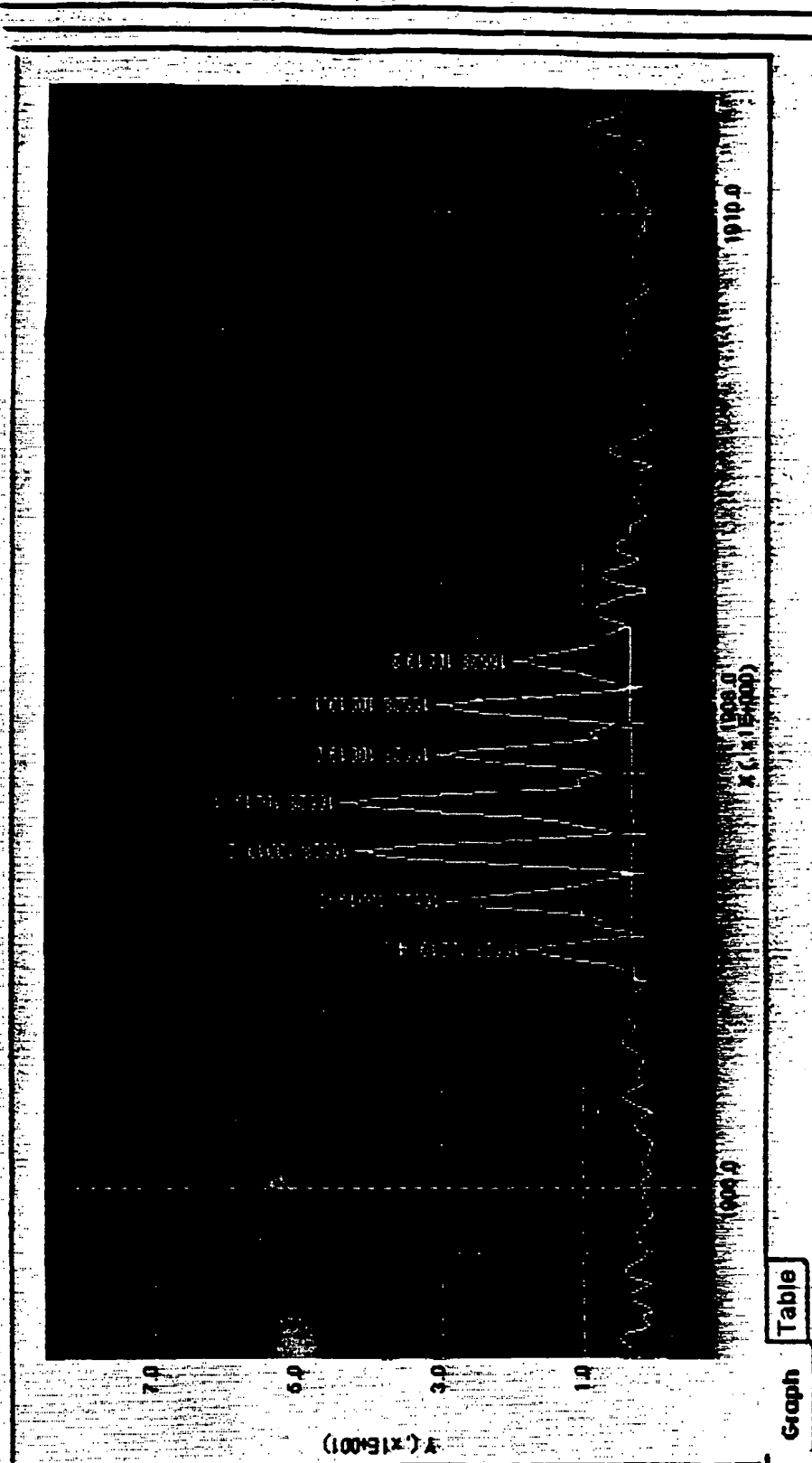
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Figure 30



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Figure 31



Graph Table

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Figure 32

N	name	apex	start	stop	height	area
1	16628-1.4	1783.710	1783.635	1783.834	14.55	1.63
2	16628-1.3	1783.909	1783.834	1783.972	60.04	5.15
3	16628-1.2	1784.109	1784.021	1784.184	115.60	11.14
4	16628-1.1	1784.308	1784.233	1784.383	167.34	15.89
5	16628-1.0	1784.508	1784.433	1784.620	133.94	14.74
6	16628-1.1	1784.707	1784.620	1784.795	136.60	13.38
7	16628-1.2	1784.907	1784.795	1784.982	82.63	8.56
8	16628-1.3	1785.107	1785.032	1785.219	57.81	5.21
9	16628-1.4	1785.306	1785.232	1785.369	32.31	2.65
10	16628-1.5	1785.506	1785.456	1785.563	17.67	1.12
11	16628.10019.4	1906.974	1906.874	1907.031	12.63	1.00
12	16628.10019.3	1907.173	1907.045	1907.273	22.54	2.11
13	16628.10019.2	1907.373	1907.287	1907.444	33.86	2.91
14	16628.10019.1	1907.572	1907.458	1907.701	34.87	3.30
15	16628.10019.0	1907.772	1907.701	1907.843	20.93	1.55
16	16628.10019.1	1907.972	1907.900	1908.043	21.03	1.55
17	16628.10019.2	1908.157	1908.086	1908.271	10.97	0.90
18	16628.4	2229.874	2229.679	2230.029	27.51	4.87
19	16628.3	2230.146	2230.029	2230.263	111.72	16.23
20	16628.2	2230.380	2230.263	2230.516	225.18	32.39
21	16628.1	2230.633	2230.516	2230.770	280.66	40.90
22	16628.0	2230.887	2230.770	2231.023	287.24	41.95
23	16628.1	2231.140	2231.023	2231.257	242.23	34.17

Graph Table

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Figure 33

